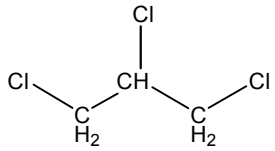
1,2,3-TRICHLOROPROPANE
CAS No. 96-18-4
First Listed in the *Eighth Report on Carcinogens*



CARCINOGENICITY

1,2,3-Trichloropropane (TCP) is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of malignant tumor formation at multiple sites in multiple species of experimental animals (NTP, 1993; Irwin et al., 1995).

TCP administered by gavage for 2 years induced tumors in male and female mice in the forestomach, liver, Harderian gland, uterus, and oral mucosa (females only), and in male and female rats in the forestomach, oral mucosa, pancreas (males only), kidney (males only), preputial gland, clitoral gland, Zymbal gland, and mammary gland (females only) (NTP, 1993; Irwin et al., 1995).

There are no adequate data available to evaluate the carcinogenicity of TCP in humans.

ADDITIONAL INFORMATION RELEVANT TO CARCINOGENESIS OR POSSIBLE MECHANISMS OF CARCINOGENESIS

TCP, when tested *in vitro,* induced gene mutations in bacteria, yeast, and mammalian cells; and sister chromatid exchanges, chromosomal aberrations, micronuclei, and morphological transformation in mammalian cells (Dean and Brooks, 1979; Sawin and Hass, 1982a,b; IARC V.63, 1995; Doherty et al., 1996). TCP was active almost exclusively in the presence but not the absence of metabolic activation or when tested using metabolically competent cells. In *in vivo* rodent studies, TCP induced DNA damage, including DNA adducts in multiple tissues of rats and mice receiving the chemical by gavage or by intraperitoneal injection (IARC V.63, 1995; La et al., 1995). TCP also induced cell proliferation in multiple tissues of rats and mice receiving the chemical by gavage or by inhalation (rats only) (NTP, 1993; Irwin et al., 1995; Johannsen, et. al., 1988). TCP has been reported as negative for the induction of dominant lethal mutations in male rats (IARC V.63, 1995). Several metabolites of TCP, including 1,3-dichloroacetone, induce genetic damage in a variety of short-term test systems (IARC V.63, 1995). This metabolite is produced by human liver microsomes, although its rate of formation is less than in rats (Weber and Snipes, 1992).

No data are available that would suggest that the mechanisms thought to account for tumor induction by TCP in experimental animals would not also operate in humans.

PROPERTIES

TCP is a clear, colorless to straw colored liquid with a strong acrid odor similar to that of chloroform or trichloroethylene. It has a melting point of -14.7°C and a boiling point of 156.8°C.

It evaporates almost as fast as water does at normal temperatures. TCP is freely soluble in alcohol, ether, and chloroform and is slightly soluble in water. It dissolves several substances, such as oils, waxes, fats, chlorinated rubber, and numerous resins. It is sensitive to prolonged exposure to light and to heat. When heated to decomposition, TCP yields highly toxic fumes of carbon monoxide, carbon dioxide, hydrogen chloride gas, phosgene gas, and other chlorinated compounds.

USE

In the past, TCP has been used mainly as a solvent and extractive agent. As a solvent, it has commonly been used as a paint and varnish remover, a cleaning and degreasing agent, and a cleaning and maintenance solvent. No current information is available to indicate that it is still used for these purposes. Currently, TCP is used as a chemical intermediate in the production of polysulfone liquid polymers and dichloropropene, synthesis of hexafluoropropylene, and as a crosslinking agent in the synthesis of polysulfides. No data were available to indicate to what extent TCP is currently used for these purposes (ATSDR, 1992f). TCP has been formulated with dichloropropenes in the manufacture of a soil fumigant D-D (OHMTADS, 1972). According to the Farm Chemicals Handbook '91 (Sine, 1991), this soil fumigant is no longer available in the United States.

PRODUCTION

The Chem Sources USA directory identified 16 U.S. and 2 foreign suppliers of TCP in 1992 (Chem Sources, 1993). The *1994 Directory of Chemical Producers United States* identified two producers of TCP (SRI, 1994). In 1985, two manufacturing facilities had a combined annual production greater than 10,000 pounds (NTP, 1993). In 1977, estimated production by four U.S. producers ranged from 21 to 110 million pounds, at least 10 million pounds of which was produced and used on-site (ATSDR, 1992f; TSCAPP, 1983). More current production volumes could not be found. There were no data available on imports or exports of TCP.

TCP may also be produced in significant quantities as a byproduct of the production of other chlorinated compounds such as dichloropropene, propylene chlorohydrin (2-chloro-1-propanol or 2-chloro-2-propanol), dichlorohydrin (1,3-dichloro-2-propanol), and glycerol (glycerin) (ATSDR, 1992f). In addition, TCP is a byproduct of the production of epichlorohydrin (IFIS, 1985).

EXPOSURE

The primary route of potential human exposure to TCP is inhalation of vapors. Other routes of exposure are ingestion and dermal contact. The National Occupational Exposure Survey (1981-1983) indicated that 492 workers, including 9 women, were potentially exposed to TCP (NIOSH, 1984). This estimate was derived from observations of the use of the actual compound (100% of total observations). The National Occupational Hazard Survey, conducted by NIOSH from 1972 to 1974, estimated that 490 workers were potentially exposed to TCP in the USA (NIOSH, 1976). Occupational exposures may result from procedures that require direct handling of the material: Purification, formulation of products, sampling and quality control,

packaging and storage, leakage of equipment, startup and shutdown procedures, maintenance, cleanup, spills, and other plant emergencies (NIOSH, 1981; cited by ATSDR, 1992f).

TCP is not a naturally occurring chemical. Releases to the environment are likely to occur as a result of its manufacture, formulation, and use as a solvent and extractive agent, paint and varnish remover, cleaning and degreasing agent, cleaning and maintenance reagent, and chemical intermediate. Releases may also occur as a result of the disposal of wastes from production of TCP and disposal of products that contain the chemical, especially at hazardous waste sites that received TCP-containing wastes (ATSDR, 1992f) such as still bottoms of epichlorohydrin manufacture (RCRA waste number K017) (IFIS, 1985). TCP has been detected in low concentrations in surface, drinking, and ground waters in various parts of the United States (ATSDR, 1992f; NTP, 1993). The Toxic Chemical Release Inventory (EPA) listed seven industrial facilities that produced, processed, or otherwise used TCP in 1996 (TRI, 1999). In compliance with the Community Right-to-Know Program, the facilities reported releases of TCP to the environment which were estimated to total 8763 lb.

Members of the general population may be exposed to low levels of TCP by ingestion of contaminated well water near a waste disposal site or agricultural lands treated with fumigants and nematocides that contain the compound as an impurity, by inhalation of contaminated air near manufacturing facilities that use or produce the compound, and by inhalation near hazardous waste disposal facilities. TCP has been detected at eight of the 1,177 U.S. EPA National Priorities List hazardous waste sites. It is uncertain how many NPL sites have been evaluated for this compound (ATSDR, 1992f).

The accumulation of TCP in shower and bathroom air during a typical shower was found to be small and was thought to be due to its low volatility (compared to other compounds studied). The low accumulation of TCP in shower and bathroom air poses less serious implications for institutional shower facilities (e.g., health clubs) than the more volatile VOCs (Little, 1992). The U.S. Department of Health and Human Services (1992) was unable to estimate the U.S. atmospheric levels of TCP, including background levels, because no data were found regarding the detection of this compound in ambient air in the United States (ATSDR, 1992f).

TCP was found in groundwater of 0.71% (8/1177) of the sites in the Contract Laboratory Program Statistical Database (CLPSD; includes data from both National Priorities List [NPL] and non-NPL sites) at a geometric mean concentration of 57.3 µg/L. It was not known how many of the 1177 sites had been actually evaluated for TCP (CLPSD, 1989, cited by ATSDR, 1992f). TCP has been found in the drinking water of New Orleans, Louisiana, Cincinnati, Ohio, and Ames, Iowa (ATSDR, 1992f, citing Keith, 1976; EPA, 1984; and EPA, 1987). TCP was found in 39% of 941 U.S. groundwater samples recorded in EPA's STORET database at a median concentration from 0.69 µg/L, at an average concentration of 1.0 µg/L, and a range from trace (below unspecified detection limit) to 2.5 µg/L (EPA STORET, 1989, cited by ATSDR, 1992f).

In February, 1976, TCP was qualitatively detected in 1 of 30 water samples taken from the Delaware, Schuylkill, and Lehigh Rivers (EPA, 1988). It was also qualitatively detected in water from Narragansett Bay, Rhode Island, sampled during the summers of 1979 and 1980, and the winters of 1980 and 1981; and in effluent from an advanced waste treatment plant in Lake Tahoe, California, in 1974 (Wakeham et al., 1983, and EPA, 1984; both cited by ATSDR, 1992f). TCP was found in grab sediment samples taken from the Grand Calumet River, Indiana,

in October and November, 1988; March, May, October, and November, 1989; and May, 1990 (Hoke et al., 1992).

Cohen et al. (1987, cited by ATSDR) found TCP at levels ranging from 0.2 to 2 ppb in soil samples from Hawaii and California during small- and large-scale retrospective studies. The compound was found at least 10 feet down in the soil profiles in Hawaii. The detection of this compound in the groundwater of hazardous waste sites suggests that it is released to soil at these sites (ATSDR, 1992f). TCP was found in soil of 0.71% of the sites of the CLPSD (8/1177) at a geometric mean concentration of 204 µg/L (CLPSD, 1989, cited by ATSDR, 1992f).

The primary removal processes of TCP from soil are volatization from near-surface soil and leaching to groundwater. TCP may persist in groundwater for a relatively long period of time and it is thought that aerobic biodegradation is a slow process in natural waters and soil (ATSDR, 1992f).

Inhalation and dermal exposures are possible during the use of consumer products such as certain paint removers. However, no data are available to indicate that the compound is currently used in consumer products or for any other purpose than as a chemical intermediate (ATSDR, 1992f). Persons whose drinking water is derived from TCP-contaminated groundwater or surface water for a long period of time may be exposed to relatively high levels this compound. The highest potential for human exposure to TCP is thought to occur during manufacture or use of TCP or TCP-containing products, such as paint- and varnish-removers and cleaners, especially when they are used in poorly ventilated areas such as in the cleaning of reactors; however, no current information indicates that TCP is still used for these purposes (ATSDR, 1992f).

Other populations with potentially high environmental exposure TCP include those that can potentially be exposed to low levels of this compound via inhalation of contaminated air at or near both unidentified and identified TCP-containing waste disposal sites and landfills. Children playing in and around these sites may also be dermally exposed to soil containing this compound adsorbed to it. However, little TCP is expected to remain in surface soil since it would be expected to leach through the soil or volatilize (ATSDR, 1992f).

REGULATIONS

TCP is regulated by EPA under the Clean Air Act (CAA), Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), Resource Conservation and Recovery Act (RCRA), and Safe Drinking Water Act (SDWA). Under CAA, the Synthetic Organic Chemicals Manufacturing Industry (SOCMI) is required to monitor equipment leaks of TCP and to develop standards of performance. The SDWA requires community and non-community water systems to be monitored for TCP. TCP is subject to the reporting requirements of Section 313 of the Emergency Planning and Community Right-to-Know Act of 1986 (EPCRA) and Section 6607 of the Pollution Prevention Act of 1990 (PPA). Section 313 of EPCRA, also referred to as Title III of the Superfund Amendments and Reauthorization Act of 1986 or SARA 313, requires the annual reporting, to EPA and the States, of releases and waste management activities for all listed chemicals manufactured, processed, or otherwise used in amounts exceeding threshold quantities by covered facilities. TCP is listed as a hazardous constituent of waste under RCRA and is subject to minimum national detection criteria in groundwater from municipal solid waste sites. SW-846 analytical methods 8010, 8021, or 8260 with Practical Quantitation Limits (PQLs) of 10, 5, or 15 µg/L, respectively are suggested. Land disposal of

liquid and nonliquid hazardous wastes containing ≥ 1000 mg/L or 1000 mg/kg (0.1%), respectively, are prohibited. A limit for TCP in waste and non-wastewater has been set at 0.85 mg/L or 28 mg/kg, respectively. A Reference Air Concentration (RAC) for TCP has been established at 0.1 $\mu g/m^3$. A reportable quantity (RQ) for TCP has not been established under CERCLA.

OSHA requires employee access to exposure and medical records relating to exposure to TCP. A PEL of 300 mg/m^3 (50 ppm) has been established as an 8 hour TWA. Although OSHA has not identified TCP as an occupational carcinogen, NIOSH recommends that it should be treated as such and that maximum respiratory protection be used. Regulations are summarized in Volume II, Table B-147.